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10/536,586	03/17/2006	Masakazu Takeuchi	082368-004500US	9187

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EXAMINER	
CHERNYSHEV, OLGA N	
ART UNIT	**PAPER NUMBER**
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/536,586	TAKEUCHI ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7 and 8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7 and 8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 May 2005* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/26/5*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *sequence alignment, two pages*.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I in the reply filed on June 22, 2007 is acknowledged.

Claims 1-5 and 7-8 are pending and under examination in the instant office action.

Sequence compliance

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821 (a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. § 1.821 through 1.825. Specifically, no sequence identification has been provided for the sequences presented in Figures 2 and 3 of the instant specification. In case these sequences are new, Applicant needs to provide a substitute computer readable form (CRF) copy of a "Sequence Listing" which includes all of the sequences that are present in the instant application and encompassed by these rules, a substitute paper copy of that "Sequence Listing", an amendment directing the entry of that paper copy into the specification, and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. § 1.821 (e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). The instant specification will also need to be amended so that it complies with 37 C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence. See M.P.E.P. 2422.04.

Specification

3. The disclosure is objected to because of the following informalities:

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, see p. 23. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. Appropriate correction is required.

Claim Objections

4. Claims 5 and 7 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claim 5 depend from claim 1, which is limited to a nucleic acid encoding a protein, while claim 5 encompasses a polypeptide, and claim 7 is directed to a nucleic acid encoding a fragment of a polypeptide while being dependent from claim 5, which is limited to a polypeptide and from claim 1, which encompasses the full length of that nucleic acid. Therefore, claims 5 and 7 can be infringed by a polypeptide and a nucleic acid, which do not infringe claim 1. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Applicant should note the "Infringement Test" for dependent claims in MPEP § 608.01(n). The test for a proper dependent claim is whether the dependent claim includes every limitation of the parent claim. A proper dependent claim shall not conceivably be infringed by anything, which would not also infringe the basic claim.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 1, 3, 5 and 7 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims fail to include any limitations, which would distinguish the claimed polynucleotides and polypeptides from those which occur in nature. In the absence of the hand of man, naturally occurring nucleic acid molecules and proteins are considered non-statutory subject matter. Diamond v. Chakrabarty, 206 USPQ 193 (1980). Filing of evidence of a new utility imparted by the increased purity of the claimed invention and amendment of the claims to recite a purity limitation, if supported by the specification, is suggested to obviate this rejection. Applicant should point to the basis in the specification for any amendment to the claims.

7. Claims 1-5 and 7-8 are further rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial credible asserted utility or a well-established utility. The instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose a specific biological role for this protein or its significance to a particular disease, disorder or physiological process, which one would wish to manipulate for a desired clinical effect.

It is clear from the instant application that the protein described therein is what is termed an "orphan protein" in the art. The DNA of the instant application has been isolated because of its similarity to a known DNA. There is little doubt that, after complete characterization, this DNA and encoded protein may be found to have a specific and substantial credible utility. This

further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediate obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion".

The instant claims are drawn to nucleic acid molecules and the protein encoded thereby of as yet undetermined function or biological significance. It is clear from the instant specification that the claimed novel nucleic acid of SEQ ID NO: 2 encodes a rat Prickle protein, R-Prickle, of SEQ ID NO: 1 (pp. 1-2 of the instant specification). More specifically, "[t]he present inventors isolated MS733 protein as a protein concentrated in a rat brain PSD fraction. [...] databases search results showed that MS733 is highly homologous to the D-prickle protein" (top at page 2). Therefore, based on the structural similarities to a different known protein, D-Prickle, of which is known that it is "a protein involved in *Drosophila* plannar cell polarity, and is known to regulate the direction of wing hair in *Drosophila*" (p. 1) and further that "the prickle

protein may participate in the formation of synaptic polarity and/or JNK signaling through its interaction with Dsh in mammals as well" (p. 1), it has been suggested that the R-Prickle of the instant invention would also possess similar biological activity as associated with processes within synapses. Numerous publications exist on a topic of predicting protein functions from structural similarities or homology to the known proteins. It is well described in the art that amino acid structure cannot necessarily predict the function of the protein: "Knowing the protein structure by itself is insufficient to annotate a number of functional classes and is also insufficient for annotating the specific details of protein function" (see Skolnick et al., Box 2 on page 36 and the whole paper). Moreover, "Structural similarity does not necessarily mean a common evolutionary origin and homologous sequences may evolve into different folds (according to current classification schemes) (See Bork et al., Current Opinion in structural Biology, 1998, 8, page 332, first column, second paragraph). Thus, according to the state of the art, functional characteristics of a protein cannot be unequivocally extrapolated from its structural characteristics.

In the absence of knowledge of the biological significance of this specific nucleic acid and encoded protein, there is no immediately obvious patentable use for the polynucleotide or the encoded protein. According to the specification of the instant application "[t]he present invention confirmed that mPrickle protein is localized in synapses, and therefore the protein can be used as a synaptic marker [or] to purify PSD-95" (p.3 of the instant specification). However, it is well settled that using a protein as a tissue marker of for purification purpose is not a specific utility. Because it could be asserted that any protein that is localized to synapses or has a common binding structure with PSD-95 could be used for these purposes and nothing about

Applicant's asserted utilities sets the claimed nucleic acids apart from any other mammalian DNA or protein, Applicant has only disclosed general uses for the claimed polynucleotides and polypeptides, not specific ones that satisfy § 101."

The instant specification further states that "mPrickle is expected to be applicable for the diagnosis of learning- and memory-related disorders such as mental deterioration and dementia in the future" (p. 3). However, the instant disclosure fails to provide any evidence or sound scientific reasoning that would support a conclusion that the instant nucleic acid or encoded protein is associated with any diseases or disorder. To employ the DNA and the protein in the future methods of diagnostic assays or treatment of clinical conditions is not a "real world" because it would eventually relate to a protein for which no biological function is known. The instant application also fails to demonstrate use of the protein as a marker for any disease or condition (which would be a real world use). Because the instant specification does not teach a biological activity of the protein, which supports a practical utility, one would not reasonably believe that the administration of drugs using "mPrickle delivery system" would prevent or treat a condition or disease, including conditions associated with NMDA receptors, as implied by the specification (p. 3).

To employ a nucleic acid or encoded polypeptide of the instant invention in any of the disclosed methods would clearly be using the claimed molecules as the object of further research, which has been determined by the courts to be a utility, which, alone, does not support patentability. Since the instant specification does not disclose a credible "real world" use for the encoded protein in their currently available form, then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-5 and 7-8 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

10. Claims 1-5 and 7-8 are further rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide encoding mammalian Prickle protein, wherein the polynucleotide comprises sense sequences associated with the Prickle protean, does not reasonably provide enablement for making antisense polynucleotide encoding a Prickle protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claim 1 is directed to a polynucleotide encoding mammalian Prickle protein, wherein the polypeptide comprises sequences which are complimentary to the sequence of SEQ ID NO: 2, the polynucleotide that encodes a polypeptide of SEQ ID NO: 1. Claims 2-5 and 7-8 are dependent claims. The prior art clearly does not teach how to produce a polypeptide by using a nucleic acid that is complementary to a nucleic acid encoding that polypeptide. The instant specification fails to provide any guidance or any working examples on how to make a

complimentary polynucleotide encoding a protein. Thus, it would require substantial amount of undue experimentation on part of a skilled artisan in order to discover how to practice Applicant's invention as currently claimed.

11. Claims 1-5 and 7-8 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 5 and 7 are directed to polynucleotides that encode polypeptides with one or more amino acid deletions, insertions, substitutions, or additions to the amino acid sequence of SEQ ID NO: 1 or fragments of SEQ ID NO: 2 or fragments of polypeptide of SEQ ID NO: 2. Claims 2, 3, 4 and 8 are dependent claims. The claims do not require that the polynucleotides and polypeptides possess any particular conserved structure or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polynucleotides and a genus of polypeptides that are defined only by sequence similarity. However, the instant specification fails to describe the entire genus of nucleic acids and proteins, which are encompassed by these claims. In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant has possession of a nucleic acid molecule which encodes a protein which has the amino acid sequence of SEQ ID NO: 1. This nucleic acid molecule has a nucleic acid sequence of SEQ ID NO: 2. The claims are drawn to fragments of proteins and nucleic acids and polynucleotides encoding proteins with proteins having deletions, insertions, substitutions, or additions within the disclosed SEQ ID NO:

1. Thus, the claims are not limited to a protein with a specific amino acid sequence or a polynucleotide with a specific nucleic acid sequence. The claims only require the claimed molecules to share some degree of structural similarity to the protein of SEQ ID NO: 1 or nucleic acid of SEQ ID NO: 2. The specification only describes a protein having the amino acid sequence of SEQ ID NO: 1 and a polynucleotide of SEQ ID NO: 2 and fails to teach or describe any other molecule which lacks these sequences and has any relevance to R-Prickle gene.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a reference to partial structure identity. There is not even identification of any particular portion of the structure that must be conserved. As stated above, it is not even clear what region of the encoded polypeptide has the activity, which is associated with biological significance of R-prickle. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at

page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides and polynucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO: 1 and polynucleotides comprising SEQ ID NO: 2, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claim 1-5 and 7-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

14. Claim 1 is rendered indefinite and ambiguous in the recitation of hybridization "under stringent conditions" as this phrase is unclear absent a statement of the conditions under which the hybridization reaction is performed. Nucleic acids that will hybridize under some hybridization conditions will not necessarily hybridize under different conditions. Without providing a precise set of hybridization conditions, in the claim or the specification, the metes and bounds of the claimed isolated nucleic acid molecule cannot be defined.

15. Claim 4 is indefinite as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Specifically, claim 4 is directed to a method of producing a protein, wherein the method is limited to one definitive step of "translating said polynucleotide". One reasonably appreciates that there are many ways/methods to produce a protein and, therefore, it is not obvious which method is intended by claim 4, as currently presented. Further, since claim 1 encompasses sequences that do not encode any polypeptide (complementary sequences), absence of method steps in claim 4 raises issues of potential lack of enablement for the claimed method.

16. Claims 2, 3, 5 and 7-8 are indefinite for being dependent from indefinite claims.

Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claims 5 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Drmanac et al., October 11, 2001, WO200175067-A2.

Claims 5 and 7 encompass fragments comprising at least eight amino acid residues of polypeptide of SEQ ID NO: 1 and polynucleotides encoding these fragments, respectively. Document of Drmanac et al. discloses polypeptide sequence which has 80.5% sequence similarity to the instant claimed molecules (see copy of the sequence alignment attached to the instant office action), thus fully anticipating the instant claimed invention.

Conclusion

19. No clam is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (571) 272-0870. The examiner can normally be reached on 8:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Y. Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR

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Primary Examiner
Art Unit 1649

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